Complete Summary

GUIDELINE TITLE

Guidelines for the management of lichen sclerosus.

BIBLIOGRAPHIC SOURCE(S)

Neill SM, Tatnall FM, Cox NH. Guidelines for the management of lichen sclerosus. Br J Dermatol 2002 Oct;147(4):640-9. [86 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Lichen sclerosus (LS), including female adult and child anogenital, male adult and child genital, and extragenital LS

GUIDELINE CATEGORY

Diagnosis
Management
Treatment

CLINICAL SPECIALTY

Dermatology
Family Practice
Internal Medicine

Obstetrics and Gynecology
Pediatrics
Surgery
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide evidence based guidance for the management of patients with lichen sclerosus (LS)

TARGET POPULATION

Patients (adults and children) with lichen sclerosus

INTERVENTIONS AND PRACTICES CONSIDERED

Clinical Assessment

1. Physical examination
2. Biopsy
3. Histopathological assessment
4. Screening for other autoimmune diseases
5. Patient follow-up

Treatment

1. Topical
    - Clobetasol propionate
    - Betamethasone dipropionate
    - Testosterone
    - Progesterone
    - Retinoids
    - Soap substitute
2. Oral
    - Potassium para-aminobenzoate
3. Physical interventions
    - Surgery
    - Laser therapy
    - Photodynamic therapy
    - Cryotherapy
4. Psychological
    - Referral to address psychosexual issues

Interventions Considered But Not Recommended

Oestrogen, ciclosporin, psoralen plus ultraviolet A (UVA) treatment, stanozolol, antimalarials, antipruritics, antihistamines, and antibiotics

MAJOR OUTCOMES CONSIDERED

- Symptom improvement
- Disease remission
- Quality of life
- Disease recurrence
- Side effects of therapy
- Disease complications
- Non-compliance with treatment
- Incidence of squamous cell carcinoma

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Evidence is searched from Medline and other medical databases and from reviews and references in publications.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

II-I: Evidence obtained from well designed controlled trials without randomization

II-ii: Evidence obtained from well designed cohort or case-control analytic studies, preferably from more than one centre or research group

II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length or comprehensiveness of follow-up or conflicts of evidence)

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation Grades

A. There is good evidence to support the use of the procedure.
B. There is fair evidence to support the use of the procedure.
C. There is poor evidence to support the use of the procedure.
D. There is fair evidence to support the rejection of the use of the procedure.
E. There is good evidence to support the rejection of the use of the procedure.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines are edited by the Therapy Guidelines and Audit Sub-committee (TGA) and subsequently returned to the task force for revision. The approved draft version is published in the quarterly British Association of Dermatologists (BAD) newsletter, and all BAD members are given the opportunity to respond, positively or negatively, but hopefully helpfully, within three months of

publication. Finalised guidelines are approved by the TGA and the Executive Committee of the BAD and finally published in the British Journal of Dermatology.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (I-IV), and strength of recommendation ratings (A-D) are defined at the end of the "Major Recommendations" field.

Investigations

The diagnosis in most patients is usually made clinically, but a confirmatory biopsy is helpful in cases where there is some clinical doubt about the diagnosis and to document any atypical features. The main differential diagnoses include lichen planus (LP), mucous membrane pemphigoid, and genital psoriasis. A skin biopsy is not always practical in children, and it is preferable to initiate their treatment without histological confirmation. A biopsy is essential in all cases that fail to respond to adequate treatment.

Histology

The classical histological features of uncomplicated lichen sclerosus (LS) include a thinned epidermis with hyperkeratosis, a wide band of homogenized collagen below the dermoepidermal junction, and a lymphocytic infiltrate beneath the homogenized area. There may be small focal areas where the inflammatory infiltrate is close to the dermoepidermal junction, similar to LP. A few patients may have a thickened epidermis; these patients tend to have complicated disease that is not so responsive to treatment and may have a higher risk in the long term of developing an associated squamous cell carcinoma (SCC).

The length of time that LS has been present cannot be determined accurately using histological parameters.

Other Investigations

Other investigations that might be indicated include a screen for other autoimmune diseases, in particular thyroid disease in women.

Management

Topical Corticosteroids

Adult Female Anogenital Lichen Sclerosus

Ideally, all women with symptomatic or active anogenital LS should be seen at least once by a dermatologist; difficult cases with complications may be best managed in a vulval clinic with a multidisciplinary team, including a dermatologist and a gynaecologist.

The recommended and accepted treatment is the ultrapotent topical corticosteroid ointment clobetasol propionate (Strength of recommendation A, Quality of Evidence II-ii). There are no randomized controlled trials providing evidence for any specific corticosteroid being the most effective or documenting that one regimen is superior to another. The regimen recommended by the authors for a newly diagnosed case is clobetasol propionate initially once a night for 4 weeks, then on alternate nights for 4 weeks and, for the final third month, twice weekly. The rationale for once daily application is based on pharmacodynamic studies showing that an ultrapotent corticosteroid needs a once daily application only.

If the patients' symptoms return with a drop in the schedule they are instructed to go back up to the frequency that was effective. A 30-g tube of clobetasol propionate should last 12 weeks and the patient is then reviewed. If the treatment has been successful the hyperkeratosis, ecchymoses, fissuring, and erosions should have resolved, but the atrophy and colour change will remain.

The clobetasol propionate is then continued and used as and when required. Most patients seem to require 30-60 grams annually. Some patients go into complete remission, requiring no further treatment. Others will continue to have flares and remissions and they are advised to use clobetasol propionate as required.

A soap substitute is also recommended, and the patient is given an information sheet on LS with instructions for the safe use of the topical corticosteroid, to try to ensure compliance.

Male Genital Lichen Sclerosus

A retrospective study of 22 men treated with clobetasol propionate documented this to be safe and effective, with significant improvement in discomfort, skin tightness, and also in urinary flow in the nine patients in whom this was affected (A, II-ii). The theoretical possibility of provoking latent human papillomavirus (HPV) infection is discussed in the original guideline document. The use of a potent topical corticosteroid often avoids the need for circumcision.

Child Anogenital Lichen Sclerosus

There is one report of betamethasone dipropionate being used with success for vulval LS in children; all patients had improvement and eight of 11 had complete remission. No maintenance therapy was required. A subsequent study of 10 girls treated with clobetasol propionate twice daily for 6-8 weeks documented similar results and lack of adverse effects during treatment or prolonged follow-up (A, II-ii).

In boys, phimosis is commonly due to LS (see above), but studies of the use of corticosteroids have not always distinguished those with LS. A prospective study of 139 boys with phimosis treated with betamethasone for 1 month documented that 80% of the 111 who completed the study had normal retractability of the foreskin after this time; 10% proceeded to circumcision as treatment failures, and 10% were having ongoing topical treatment (A, II-ii).

An ultrapotent topical corticosteroid may avoid a circumcision in some cases of preputial phimosis.

Extragenital Lichen Sclerosus

Clobetasol propionate, with or without occlusion, is the first-line treatment. This is used once daily, as and when required. In general, extragenital lesions are not as responsive as genital disease to the potent topical corticosteroid (A, III).

Testosterone and Other Hormones

Adult Female Anogenital Lichen Sclerosus

Older studies have documented benefit from use of topical testosterone in vulval dystrophy (presumably some of these cases were LS), including one controlled study in LS that documented greater benefit in the active treatment group. However, more recent research has documented that it is not as effective as clobetasol propionate and is no more effective than an emollient. In the maintenance of remission after topical corticosteroid it was actually worse than an emollient control (D, II-i). Topical testosterone is expensive and with overuse can lead to virilization.

Topical progesterone has also been reported to be effective (C, IV).

Male Genital Lichen Sclerosus

Testosterone has also been used topically (2.5% ointment) for male genital LS (C, IV).

Child Anogenital Lichen Sclerosus

Topical oestrogen was reported to be beneficial in four girls, improving the histological features and itch (in the three who had this symptom). However, the magnitude of benefit is uncertain as this report stated that the overall clinical improvement was 20%, and no comparative trials are available.

Surgery, Laser, Photodynamic Therapy and Cryotherapy

Adult Female Anogenital Lichen Sclerosus

There is no indication for removal of vulval tissue in the management of uncomplicated LS, and surgery should be used exclusively for malignancy and postinflammatory sequelae.

In one study, nine of 12 patients with severe itch due to vulval LS unresponsive to topical treatment responded to cryotherapy, 50% for 3 years (C, III).

In an open study of photodynamic therapy for vulval LS (topical 5-aminolaevulinic acid, argon laser light, one to three treatments), 10 of 12 patients had significant improvement. Laser treatment has also been used with some success (C, III).

Male Genital Lichen Sclerosus

The role of surgery is better documented for penile LS, either to improve symptoms due to phimosis, which has failed to respond to a trial of an ultrapotent topical corticosteroid, or symptoms due to meatal stenosis. Two reviews (52 patients in total) document satisfactory results from circumcision for LS of the foreskin, and meatal dilatation, meatotomy, or meatoplasty for meatal stenosis.

Laser treatment has generally employed the carbon dioxide laser, and may have a role in the treatment of meatal stenosis (B, III).

Child Anogenital Lichen Sclerosus

Surgical treatment of childhood phimosis by circumcision has demonstrated the presence of LS in a high proportion of cases, but topical corticosteroids should be used first.

Extragenital Lichen Sclerosus

Shave (tangential) excision has been used, and carbon dioxide laser has been reported to produce an improvement in symptoms and appearance of lesions.

A case of extragenital LS in a child has been successfully treated with low-dose ultraviolet (UV) A1 phototherapy

Other Treatments

Ciclosporin

A pilot trial of topical ciclosporin failed to have any beneficial effect clinically or histologically on five cases of vulval LS (D, III).

Retinoids

There is no evidence that these are particularly effective in uncomplicated LS but there is some evidence that they may have a role in complicated disease that does not respond to an ultrapotent corticosteroid, including one long-term placebo controlled study. However, this study only documented benefit in 14 of 22 evaluable patients as well as in six of 24 controls, and only 46 of 78 patients could be evaluated. Use of topical retinoids is accompanied by the problem of irritancy (C, I).

Potassium Para-aminobenzoate

A report of five patients with LS at various sites, and resistant to numerous other therapies, documented good improvement in all five (dose 4-24 grams daily in divided doses) (C, III).

Others

There are reports of benefits from psoralen plus UVA treatment, stanozolol, antimalarials, antipruritic and antihistamine agents such as oxatomide, and various antibiotics (for which the main rationale is the uncertain link with Borrelia infection). These and others are summarized elsewhere, but must all be viewed as less well proven or as anecdotal.

Treatment Failure

If treatment with topical corticosteroids fails to bring LS under control then it is important to consider the following:

1. Non-compliance. Sometimes patients may be alarmed at the warnings on the package insert warning against the use of a topical corticosteroid in the anogenital area and they will then not use the preparation. Also, very elderly patients disabled with poor eyesight and limited mobility may not be able to apply the medication appropriately.
2. Is the diagnosis correct, or is there an added problem such as the development of a contact allergy to the medication or is there another superimposed condition (e.g., secondary candidiasis, intraepithelial neoplasia, malignancy, psoriasis, or mucous membrane pemphigoid)?
3. Is the LS in fact treated, but the patient is still symptomatic because they have developed a secondary sensory problem, dysaesthetic vulvodynia, or are experiencing problems with intercourse that they may feel too shy to discuss?
4. Is the problem mechanical due to scarring (e.g., severe phimosis or meatal stenosis in males) in which case surgery may be indicated?

Follow-up

The risk of malignancy in uncomplicated genital LS that has been diagnosed and treated appropriately is very small. If malignancy occurs it does so rapidly. Early detection would require 3-monthly follow-up consultations; this is generally impossible in the U.K. due to the constraints of the National Health Service system.

The authors suggest two follow-up visits after the initial consultation: (i) at 3 months to assess response to treatment and to ensure that the patient is using the topical corticosteroid appropriately and judiciously, and (ii) if response has been satisfactory, a final assessment 6 months later to ensure that the patient is confident in treating their problem and to take the opportunity to discuss any residual problems that the patient might have before discharge back to the care of their primary physician. If patients continue to use a topical corticosteroid it is suggested that they see their primary care physician once yearly. Instruction should be given to the patient at the time of their discharge from the clinic warning them that any persistent ulceration or new growth must be reported to their family practitioner who will then make an urgent referral back to an appropriate specialist.

Long-term follow up is, however, required for patients with LS that continues to be poorly controlled. These patients usually have LS with a histological pattern that has features of both LS and LP with squamous cell hyperplasia. Clinically, these patients seem to have an overlap syndrome and their disease runs a

relentless course despite trials of various therapies, and a small percentage does go on to develop one or more SCCs.

It is important to biopsy persistent ulcers, erosions, hyperkeratosis, and erythematous zones, whether present at initial presentation or subsequently, to exclude intraepithelial neoplasia or invasive SCC.

Summary of Recommendations and Conclusions

- An ultrapotent topical corticosteroid is the first-line treatment for LS in either sex at any site, but there are no randomized controlled trials comparing corticosteroid potency, frequency of application, and duration of treatment.
- Asymptomatic patients with evidence of clinically active LS (i.e., ecchymosis, hyperkeratosis, and progressing atrophy) should be treated.
- Anogenital LS is associated with SCC, but the development of this complication is rare in clinical practice (5% or less). It is not yet known whether treatment will lessen the long-term risk of malignant change.
- Long-term follow up in a specialized clinic is unnecessary for uncomplicated disease that is well controlled clinically using small amounts of a topical corticosteroid, and follow up should be reserved for patients with complicated LS that is unresponsive to treatment and those patients who have persistent disease with history of a previous SCC.
- Surgical intervention is indicated only for the complications of scarring or the development of malignancy.
- Any psychosexual issues should be addressed if appropriate and referral made to practitioners experienced in this field if indicated.

Definitions:

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

II-I: Evidence obtained from well designed controlled trials without randomization

II-ii: Evidence obtained from well designed cohort or case-control analytic studies, preferably from more than one centre or research group

II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length or comprehensiveness of follow-up or conflicts of evidence)

Recommendation Grades

A. There is good evidence to support the use of the procedure.
B. There is fair evidence to support the use of the procedure.
C. There is poor evidence to support the use of the procedure.
D. There is fair evidence to support the rejection of the use of the procedure.
E. There is good evidence to support the rejection of the use of the procedure.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Consistent high level quality of care for patients with lichen sclerosus (LS)

POTENTIAL HARMS

- Topical testosterone may result in virilization in women.
- Use of topical retinoids is accompanied by the problems of irritancy.
- There is a theoretical possibility that topical steroids may provoke latent oncogenic human papillomavirus (HPV).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines have been prepared for dermatologists on behalf of the British Association of Dermatologists and reflect the best data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.
- The aim of the British Association of Dermatologists is to provide guidelines for the management of skin diseases using as much evidence-based data as possible. There are few published randomized controlled trials to support the above guidelines for the management of lichen sclerosus (LS); the recommendations made are those that are currently considered best practice but will be modified at intervals in the light of new evidence.

- Appraising and grading the evidence for the treatment of LS is not easy, particularly as it is a disorder in which many treatments have a large placebo effect; additionally, disease definition has been unreliable or unclear in some of the reports so it is possible that "therapy-resistant cases" may have had some atypical features.
- It is important that these guidelines are used appropriately in that they can only assist the practitioner and cannot be used to mandate, authorise, or outlaw treatment options. Of course it is the responsibility of the practising clinician to interpret the application of guidelines, taking into account local circumstances.
- Guidelines are inherently a fluid, dynamic process and will be updated on the British Association of Dermatologists (BAD) Web site on a regular basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Audit Points

- Has a biopsy been performed in patients with clinically active disease that is unresponsive to adequate treatment with an ultrapotent topical corticosteroid?
- Are follow-up arrangements in place for patients with ongoing symptomatic disease?
- Are patients with genital lichen sclerosus (LS) aware that any persistent ulcer, erosion, or new growth within the affected skin needs to be reported?
- Has a topical corticosteroid of adequate potency and duration been used prior to surgery in males with symptomatic preputial tightening?

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Neill SM, Tatnall FM, Cox NH. Guidelines for the management of lichen sclerosus. Br J Dermatol 2002 Oct;147(4):640-9. [86 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Oct

GUIDELINE DEVELOPER(S)

British Association of Dermatologists

SOURCE(S) OF FUNDING

British Association of Dermatologists

GUIDELINE COMMITTEE

British Association of Dermatologists Therapy Guidelines and Audit Subcommittee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Association for Genitourinary Medicine - Medical Specialty Society
Medical Society for the Study of Venereal Diseases - Disease Specific Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the British Association of Dermatologists Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Griffiths CE. The British Association of Dermatologists guidelines for the management of skin disease Br J Dermatol. 1999 Sep;141(3):396-7.

Electronic copies: Available in Portable Document Format (PDF) from the British Association of Dermatologists Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 21, 2005. The information was verified by the guideline developer on August 2, 2005.

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